Isoniazid prevented active tuberculosis in patients with HIV treated with antiretroviral therapy

Clinical impact ratings: ★★★★★★ ★★★★★★ ★★★★★★ ★★★★★★ ★★★★★★ ★★★★★★

**Question**
In patients who have HIV infection and are receiving antiretroviral therapy (ART), what is the efficacy of isoniazid (INH) for preventing active tuberculosis (TB)?

**Methods**

**Design:** Randomized placebo-controlled trial. ClinicalTrials.gov NCT00463086.

**Allocation:** Unclear allocation concealment.*

**Blinding:** Blinded? (patients, clinicians, and pharmacy staff).

**Follow-up period:** Up to 3.7 years (median 2.5 y).

**Setting:** Ubuntu ART clinic in Cape Town, South Africa.

**Patients:** 1369 adults ≥ 18 years of age (median age 34 y, 75% women) who had HIV infection treated with ART and baseline TB symptom screening and sputum mycobacterial culture. Exclusion criteria included proven or suspected active TB, past or present treatment of latent TB infection (LTBI), use of fluoroquinolones or other antibiotics with anti-TB activity, intolerance to INH, or grade 3 or 4 alanine transaminase or peripheral neuropathy.

**Intervention:** INH, 200 mg/d for body weight < 50 kg or 300 mg/d for body weight ≥ 50 kg (n = 680), or placebo (n = 689), added to pyridoxine, 25 mg, for 12 months (up to 15 mo).

**Outcomes:** TB (definite, probable, or possible). Secondary outcomes were all-cause mortality and study drug discontinuation due to adverse drug reactions.

**Patient follow-up:** 81% (modified intention-to-treat analysis).

**Main results**
INH reduced risk for TB, but not death, compared with placebo (Table). INH did not increase risk for study drug discontinuation due to adverse events more than placebo (4% vs 3%, relative risk 1.1, 95% CI 0.84 to 1.42).

**Conclusion**
In patients who have HIV infection and are receiving antiretroviral therapy, isoniazid reduced risk for active tuberculosis.

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### Outcomes Event rate/100 person-y At a median 2.5 y

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Event rate/100 person-y</th>
<th>Isoniazid</th>
<th>Placebo</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis</td>
<td>2.3</td>
<td>3.6</td>
<td>35%</td>
<td>29 (18 to 264)</td>
<td></td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>0.9</td>
<td>1.2</td>
<td>28% (-33 to 66)</td>
<td>Not significant</td>
<td></td>
</tr>
</tbody>
</table>

*Abbreviations defined in Glossary. RRR, NNT, and CI calculated from event rates and hazard ratios in article.

*Adjusted for time-updated CD4 count.

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**References**